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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,651	01/27/2004	Ronald A. Beyerinck	PC23195B	4574

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
EASTERN POINT ROAD
GROTON, CT 06340

EXAMINER	
SASAN, ARADHANA	
ART UNIT	**PAPER NUMBER**
1615	

NOTIFICATION DATE	DELIVERY MODE
04/10/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

~IPGSGro@pfizer.com

Office Action Summary	Application No.	Applicant(s)	
	10/766,651	BEYERINCK ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-26,30,34-37 and 39-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-26,30,34-37 and 39-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 2/12/08 are acknowledged.

2. Claims 27-29, 31-33 and 38 were cancelled. Claims 22, 34 and 39-43 were amended.

3. Claims 22-26, 30, 34-37 and 39-43 are included in the prosecution.

Response to Arguments

Rejection of claims under 35 USC § 103(a)

4. Applicant's arguments, see Page 5, filed 2/12/08, with respect to the rejection of claims 22-25 under 35 U.S.C. 103(a) as being unpatentable over Illum (WO 96/41632), the rejection of claims 26-27 under 35 U.S.C. 103(a) as being unpatentable over Illum (WO 96/41632) in view of Chang et al. (US 6,121,283), the rejection of claims 28-37 under 35 U.S.C. 103(a) as being unpatentable over Illum (WO 96/41632) in view of Chang et al. (US 6,121,283) and further in view of Nakamichi et al. (US 5,456,923), and the rejection of claims 38-43 under 35 U.S.C. 103(a) as being unpatentable over Illum (WO 96/41632) in view of Gombotz et al. (US 5,019,400) have been fully considered. Applicant amended claim 22 to incorporate claims 29, 32 and 38.

Applicants argue that combining the references of record would not produce the claimed invention. Moreover, a skilled worker would not be motivated to combine these references due to the differences in manufacturing technologies. This is not found persuasive because the claimed elements are taught by Illum, Chang, Nakamichi and Gombotz, and one of ordinary skill in the art could have combined the elements and the

combination would have yielded predictable results. See *KSR International Co. v. Teleflex Inc.*, 550 U.S. - , 82 USPQ2d 1385 (2007). Amended claim 22 is in the form of a product-by-process claim, which is considered a product claim by the Office. Applicants are reminded that process limitations cannot impart patentability to a product that is not patentably distinguished over the prior art.

However, upon further consideration, new grounds of rejection, necessitated by applicant's amendment, based on the combination of references Illum, Chang, Nakamichi and Gombotz follow. Since this new ground of rejection was necessitated by applicant's amendment, the rejection is made final.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 22-25, 30, 34-37 and 39-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (WO 96/41632) in view of Chang et al. (US 6,121,283) and further in view of Nakamichi et al. (US 5,456,923) and Gombotz et al. (US 5,019,400).

The claimed invention is a composition comprising a plurality of solid amorphous dispersion particles comprising a substantially amorphous drug and a polymer selected from the group consisting of hydroxypropyl methyl cellulose, hydroxypropyl cellulose, carboxymethyl ethyl cellulose, hydroxypropyl methyl cellulose acetate succinate,

hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, cellulose acetate trimellitate, polyvinyl alcohols that have at least a portion of their repeat units in hydrolyzed form, polyvinyl pyrrolidone, poloxamers, and blends thereof wherein the particles have an average diameter of at least 40 μm and a bulk specific volume of less than 5 mL/g, and wherein at least 80 vol% of the particles have diameters of greater than 10 μm and wherein the particles are formed by a spray drying process. The process comprises the steps (a) forming a feed solution comprising the drug, the polymer, and a solvent; (b) directing the feed solution to a spray-drying apparatus; (c) atomizing the feed solution into droplets in the spray-drying apparatus; and (d) contacting the droplets with a drying gas to form the particles.

Illum teaches a pharmaceutical composition comprising an anti migraine compound and starch microspheres (Abstract). A therapeutically effective amount of a compound is loaded on starch microspheres (Page 3, lines 10-13). "At least 80% (measured by weight) of the microspheres should have a diameter ranging between about 10 and 200μm … (and) more than 90% (measured by weight) of the microspheres should have a diameter between 10 and 200μm" (Page 3, lines 32-36).

Illum does not expressly teach the bulk specific volume of less than 5ml/g or a cellulosic polymer in the composition.

Nakamichi teaches a solid dispersion produced without heating a drug and polymer to or beyond their melting points and without using an organic solvent for dissolving both components (Abstract). "The term 'solid dispersion' is used … to mean an drug-containing pharmaceutical bulk substance comprising the drug dissolved or

dispersed in a polymer" (Col. 1, lines 14-16). Hydroxypropylmethylcellulose acetate succinate is disclosed as a polymer used in the solid dispersion (Col. 2, line 43).

Illum does not expressly teach the dispersion formed by a spray drying process.

Gombotz teaches: "a variety of techniques are known by which active agents can be incorporated into polymeric microspheres. An example is spray drying. In spray drying, the polymer and active agent are mixed together in a solvent for the polymer, then the solvent is evaporated by spraying the solution, leaving polymeric droplets containing the active agent" (Col. 1, lines 9-15).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a pharmaceutical composition comprising microspheres loaded with a drug, as suggested by Illum, combine it with the hydroxypropylmethylcellulose acetate succinate as the polymer in the dispersion, as taught by Nakamichi, further combine it with the spray drying technique for mixing drug into polymer microspheres, as disclosed by Gombotz, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Nakamichi teaches that "solid dispersions are of use for an enhanced solubility of drugs or for controlling the rate of release of a drug from a dosage form or improving the bioavailability of drugs, thus being of significant commercial value" (Col. 1, lines 19-22) and the spray drying technique disclosed by Gombotz is an alternate process to making dispersions of drug and polymer and would be obvious to try with a reasonable expectation of success.

Regarding instant claim 22, the limitation of the substantially amorphous drug would have been obvious over the drugs and active ingredients taught by Illum, Nakamichi and Gombotz. The limitation of the polymer would have been obvious over the hydroxypropylmethylcellulose acetate succinate taught by Nakamichi. The limitation of the spray drying process would have been obvious over the spray drying teaching of Gombotz.

Regarding instant claims 22 and 25, the limitation of the bulk specific volume of less than 5ml/g would have been obvious to one skilled in the art as a physical property of the particles. One skilled in the art would modify the components of the composition and measure the bulk specific volume of the particles during the process of routine experimentation as a physical indicator and the recited bulk specific volume would have been an obvious variant absent evidence of criticality or unexpected results.

Regarding instant claims 22-24, the limitation of the particle diameter would have been obvious to one skilled in the art over the particle size teaching of Illum.

Regarding instant claim 30, the limitation of the hydroxypropylmethylcellulose acetate succinate would have been obvious to one skilled in the art over the hydroxypropylmethylcellulose acetate succinate teaching of Nakamichi.

Regarding instant claim 34, the polymer would have been obvious to one skilled in the art over the hydroxypropylmethylcellulose acetate succinate teaching of Nakamichi. As shown in Test Example 1, the dispersion of the drug in the polymer (hydroxypropylmethylcellulose acetate succinate) has the function of acting as an enteric coated product (Col. 9, lines 25-38). Therefore, the polymer allows the protection

of the drug or concentration enhancement of the drug when administered in a particular use environment.

Regarding instant claims 35-37, the maximum drug concentration enhancement of at least 1.25 fold would have been obvious because one skilled in the art would modify the composition as taught by Illum, in view of Nakamichi, in order to optimize the desired drug delivery rate or concentration, area under the drug concentration versus time curve, and relative bioavailability of the drug in the target environment and compare it to a control composition during the process of routine experimentation.

Regarding instant claim 38, the composition made by the process of spray drying would have been obvious to one skilled in the art over the spray drying teaching of Gombotz.

Regarding instant claims 39, 40, and 41, the average droplet diameter, D_{10} and D_{90} limitations would have been obvious because one skilled in the art would measure the droplet diameter and determine the D_{10} and D_{90} during the process of routine optimization and the recited diameters would have been obvious variants absent any evidence of criticality or unexpected results.

Regarding instant claims 42 and 43, the span limitations would have been obvious because one skilled in the art would measure and optimize the particle diameter ranges and further calculate the span during the process of routine experimentation. The recited span values would have been obvious variants absent any evidence of criticality or unexpected results.

7. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (WO 96/41632) in view of Chang et al. (US 6,121,283).

The teaching of Illum is stated above.

Illum does not expressly teach the drug as cholesteryl ester transfer protein inhibitor.

Chang teaches pharmaceutical compositions suitable for the treatment of conditions including atherosclerosis, hypercholesterolemia, hyperglyceridemia, and hyperlipidemia (Col. 9, lines 10-13). The compounds of the invention may be used in conjunction with other pharmaceutical agents, including other lipid lowering agents such as CETP inhibitors (Col. 9, lines 41-47). "Any compound having activity as a CETP inhibitor can serve as the second compound in the combination therapy … The term CETP inhibitor refers to compounds which inhibit the cholesteryl ester transfer protein (CETP) mediated transport of various cholesteryl esters and triglycerides from high density lipoprotein (HDL) to low density lipoprotein (LDL) and very low density lipoprotein (VLDL)" (Col. 10, line 66 to Col. 11, line 6).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a pharmaceutical composition comprising microspheres loaded with a drug, as suggested by Illum, and combine it with the CETP inhibitor as the drug, as taught by Chang, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Chang teaches dosage forms of the compounds (including CETP inhibitors) such as oral dosage forms, tablets, pills, and capsules (Col. 31, lines 5-34). One skilled in the art

would use the drug in the microsphere composition taught by Illum and have a reasonable expectation of success.

Conclusion

8. No claims are allowed.

9. **THIS ACTION IS MADE FINAL.** The new grounds of rejection were necessitated by Applicant's amendment. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/Michael P Woodward/
Supervisory Patent Examiner, Art Unit 1615